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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/530,421	04/05/2005	Peter G. Schultz	54A-000170US	6734

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EXAMINER	
GEBREYESUS, KAGNEW H	
ART UNIT	PAPER NUMBER
1656	
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/530,421	SCHULTZ ET AL.	
	Examiner	Art Unit	
	Kagnew H. Gebreyesus	1656	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *15 May 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-10 and 12-27* is/are pending in the application.

4a) Of the above claim(s) *18-27* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-10 and 12-16* is/are rejected.

7)☒ Claim(s) *17* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *1/19/07 &1/25/07*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicant's election with traverse of Group I comprising claims 2-8 and 17 in the reply filed on May 15, 2007 is acknowledged. Claims 1, 3, 4, 7, 9, 14, 15, 23 and 24 are amended. Claims 11 and 28 have been cancelled. Claims 2-8 and 17 are present for examination.

Priority

Acknowledgment is made to this application which is a 371 of PCT/US03/32576 10/15/2003 which claims benefit of 60/419,265 10/16/2002 and claims benefit of 60/420,990 10/23/2002

Information Disclosure Statement

The information disclosure statement filed on April 05, 2005 for which a copy of the patent publication has been submitted in this application has been considered as shown by the Examiners signature next to each reference.

Oath/Declaration

The oath or declaration submitted on April 05, 2005 has been reviewed and is in compliance with 37 CFR 1.56.

Specification

The specification is objected to for an unclear incorporation by reference. In paragraphs [0091] and [0098], [0141], [0184] reference to a related case by attorney docket number is unclear. The Examiner suggests use of either the Patent Application Publication number of the other application (preferable) or the application number for clarity. Correction is required.

Response to traversal

Applicants argument and further claim amendment regarding the restriction requirement has been carefully considered. However Applicants arguments is not found persuasive for the

following reasons:

In the first instance, Applicants argue:

"...the Examiner does not state explicitly what groups are linked to claim 1. However, it appears that the Examiner intends to join Groups 2 and 3, in the event that claim 1 is found allowable. Thus, if claim 1 is found allowable as it applies to SEQ ID NO: 18, claims 1-8 and 17 will also be examined as they apply to SEQ ID NOS: 19 and 20. This end result will effectively resemble an election of species requirement. Applicants respectfully request clarification from the Examiner..."

However, it is clearly stated that claim 1 links the inventions in claims 2-8 and 17 which are found in Groups 1-3, thus if the invention in Group 1 is allowable group 2 and 3 comprising the special technical feature would be examined.

Furthermore Applicants argue:

> "...In the Office Action, the Examiner found alleged lack of Unity of Invention because the technical feature of the orthogonal aminoacyl-tRNA synthetase (O-RS) is allegedly not a special technical feature defined by PCT Rule 13.2.
>
> Applicants disagree, and point out that the presently amended form of the claims remove, any ambiguity in interpretation of the claim language that may have been present, and may have "resulted in the finding of lack of Unity of Invention. For example, all claims now require that the amino acid be p-acetyl-L-phenylalanine...

Furthermore Applicants argue:

"...The Examiner states that the O-RS sequences of SEQ ID NOS: 18, 19 and 20 are distinct structures with distinct functions. Applicants disagree. The three novel synthetase variants are highly related to each other, where they differ from each other at not more than five amino acid positions. Furthermore, each of these novel polypeptides has the same function, i.e., charges an orthogonal tRNA with the keto amino acid p-acetyl-L-phenylalanine. Searching these three sequences is not an undue burden..."

Applicant's argument has been considered carefully. In the first instance, Applicants are reminded that the reasoning provided in the previous Office Action for lack of unity of the

claimed invention was based on the claims as originally presented. The claims are now amended to recite that the orthogonal tRNA synthetases, including SEQ ID NO: 18, 19 and 20, sequences used as points of references for the degree of efficiency, aminoacylate a corresponding orthogonal tRNA with the specific keto group containing unnatural amino acid, p-acetyl-L-phenylalanine.

Based on the newly amended claims, the special technical feature in claim 1 is drawn to any orthogonal tRNA synthetase molecule that can aminoacylate an O-tRNA with p-acetyl-L-phenylalanine. This is because the invention first claimed in the application is drawn to ORS molecules defined only by relative degree of efficiency i.e. relative function with no structural disclosure for the ORS molecules per se. The claim recites an ORS with at least 50% efficiency relative to the efficiency of the ORS of SEQ ID NO: 18-20, sequences implicitly assigned an arbitrary value of 100% efficiency. Therefore, SEQ ID NO: 18-20 are not considered the special technical features of the invention. The technical feature of claim 1 is any ORS with any structure that can aminoacylate an OtRNA with p-acetyl-L-phenylalanine with efficiency of at least 50% relative to an undefined arbitrary value.

This technical feature however, is not a special technical feature because US 7,045,337 B2 (Schultz et al) filed on April 19, 2002 teaches a cell composition comprising an ORS that aminoacylates an OtRNA with p-acetyl-L-phenylalanine.

Applicants argue:

> "...The three novel synthetase variants are highly related to each other, where they differ from each other at not more than five amino acid positions. Furthermore, each of these novel polypeptides has the same function, i.e., charges an orthogonal tRNA with the keto

amino acid p-acetyl-L-phenylalanine. Searching these three sequences is not an undue burden..."

However as stated above, the technical feature of claim 1 is not a special technical feature because SEQ ID NO: 18-20 are not the technical features as presently claimed. In addition, SEQ ID NO: 18-20 are structurally distinct and the search for each of the sequences would incur costly resources in multiple databases including searches in patent and non-patent literatures. Thus co-examination of the inventions in all the groups (1-12) as it applies to SEQ ID NO: 18-20 in one patent application would be a serious burden.

However upon further reconsideration, Group 1-6 (comprising claims 1-10 and claims 12-17) will be examined together as it applies to the ORS of SEQ ID NO: 18 because these claims are deemed to comprise overlapping subject matter.

Furthermore if the products claimed in Groups 1-6 are allowed the process of using the product (group 10-12) will also be rejoined.

Claims 1-10, 12-17 will be examined herewith.

Claim Objections

Claims 1-10,12-17 are objected to because of the following informalities: These claims contain non-elected subject matter because they include SEQ ID NO: 19 and 20. Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-10, 12-16 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter, which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The specification teaches a few structures (SEQ ID NO: 18-20) that can function to aminoacylate an OtRNA with p-acetyl-phenylalanine. However these claims recite a composition or a cell comprising a genus of ORS molecules that can aminoacylate an OtRNA with at least 50% efficiency relative to the efficiency of an ORS of SEQ ID NO: 18 (1, 3-9, 15). Claims 1, 3-9, 15 are described only functionally and no structural correlation can be inferred from the recited "ORS with at least 50% efficiency relative to the structure of SEQ ID NO: 18". Furthermore, claims 2, 10, 12-14 recite ORS of SEQ ID NO: 18 and conservative variants thereof. The specification teaches that "conservative variants" can comprise 1, 2, 3, 4, 5 or more amino acid variations relative to SEQ ID NO: 18. Thus any number of variations is encompassed in the claims.

The court of appeals for the Federal Circuit has held that a "written description of an invention involving a chemical genus, like a description of a chemical species, 'requires a precise definition, such as structure, formula [or] chemical name, 'of the claimed subject matter sufficient to distinguish it from other material. " For claims drawn to a genus, MPEP § 2163 states the written description required for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice, reduction to

drawings, or by a disclosure of relevant identifying characteristics, sufficient to show the applicant was in possession of the claimed genus. MPEP § 2163 states that a representative number of species means that the species, which are adequately described, are representative of the entire genus.

Thus, when there is substantial variation within the genus, one must describe a sufficient variety of species to reflect the variation within the genus.

In this case, the specification discloses a few representative species of the genus of claimed polypeptides, i.e. SEQ ID NO: 18-20. However the specification fails to describe any other representative species by any identifying characteristics or property other than the functionality of aminoacylating an OtRNA with p-acetyl-phenylalanine. Claims 1, 3-9 and 15 are functionally characterized and claims 2, 10-14 and 16 comprise unlimited modifications of SEQ ID NO: 18 by virtue of the recitation "conservative variations thereof.

While MPEP § 2163 acknowledges that in certain situations "one species adequately supports a genus", it also acknowledges that "[f]or inventions in an unpredictable art, adequate written description of a genus which embraces widely variant species cannot be achieved by disclosing only a few species within the genus." In the instant case the recited genus of ORS molecules encompass species widely variant with respect to their structures, which include aminoacyl tRNA synthetase molecule with any number and combination of alterations, including any addition, substitution, deletion and/or insertion with no structural limitation. The disclosure of the species of SEQ ID NO: 18 is insufficient to be representative of the attributes and features of all species encompassed by the claimed genus of ORS molecules.

Thus the skilled artisan would not know what the structure of an ORS that can aminoacylate an OtRNA with p-acetyl-phenylalanine with an efficiency of 63%, 92%, 107%, 120% etc.:. relative to SEQ ID NO: 18 would look like because the specification does not disclose any structure/function correlation between the genus of functionally claimed ORS and the structure of these ORSs. For example the specification does not teach which residues in a given ORS among the genus claimed are critical in imparting the capability to aminoacylate a corresponding OtRNA with p-acetyl-phenylalanine. In addition claims 1, 3-9 and 15 do not recite the type of tRNA synthetase from which the claimed genus of ORS originates (tyrosyl tRNA synthetase, phenylalanyl tRNA synthetase etc).

Given this lack of description of representative species encompassed by the claimed genus, the specification fails to sufficiently describe the invention in such full, clear, concise, and exact terms that a skilled artisan would recognize that applicants were in possession of the claimed invention.

Claims 1-10, 12-16 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for ORS molecule of SEQ ID NO: 18 that can aminoacylate an OtRNA with p-acetyl-phenylalanine, does not reasonably provide enablement for any ORS molecule comprising any ORS from any source and with any structure as encompassed in claims 1, 3-9 and 15 or does not provide enablement for any ORS comprising any number of amino acid modifications to the ORS of SEQ ID NO: 18 (claims 2, 10-14 and 16). The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with the above claims.

Factors to be considered in determining whether undue experimentation is required, are summarized ln re Wands (858 F.2d 731, 8 USPQ 2nd 1400 (Fed. Cir. 1988). The Wands factors are: (a) the quantity of experimentation necessary, (b) the amount of direction or guidance presented, (c) the presence or absence of working example, (d) the nature of the invention, (e) the state of the prior art, (f) the relative skill of those in the art, (g) the predictability or unpredictability of the art, and (h) the breadth of the claim.

The nature and breadth of the claims encompasses any ORS from any source that can aminoacylate a corresponding OtRNA with p-acetyl-phenylalanine (clam 1, 3-9, 15) or any polypeptide variant showing any degree of sequence identity (by virtue of the definition of "conservative variant") to ORS polypeptide of SEQ ID NO: 18 (claim 2, 10, 12-14, 16). The specification provides guidance and examples of making a few ORS molecules that can aminoacylate an OtRNA with p-acetyl-phenylalanine. However, the specification does not teach the specific structure of all possible ORS molecules from any source that can aminoacylate a corresponding OtRNA with p-acetyl-phenylalanine. Furthermore the specification does not teach how to make any polypeptide comprising any modification to the polypeptide sequence of SEQ ID NO: 18 (claim 2, 10, 12-14, 16) while retaining the capacity to aminoacylate an OtRNA with p-acetyl-phenylalanine.

The standard for meeting the enablement requirement is whether one of skill in the art can make the invention without undue experimentation. The amount of experimentation to make the claimed invention is enormous and undue. Such experimentation entails performing any

genetic mutation on any polypeptide sequence encoding any ORS gene from any biological source and determining whether the genetic mutation results in an ORS polypeptide that can aminoacylates a tRNA with p-acetyl-phenylalanine. Thus, searching for the specific biological source and the structures of the ORS encompassed and the specific genetic modification which will result in aminoacylation of a tRNA with p-acetyl-phenylalanine is enormous.

The Examiner finds that one skilled in the art would require additional guidance, such as information regarding the specific source and structure of the claimed ORS molecules with the capacity to aminoacylate an OtRNA with p-acetyl-phenylalanine. Furthermore additional guidance are required with respect to the modification(s) made to the ORS of SEQ ID NO:18 while retaining the ability to aminoacylate an OtRNA with p-acetyl phenylalanine. However the specification does not teach regions or specific residues in any ORS which are critical for the specific characteristics desired i.e. the ability to aminoacylate an OtRNA with p-acetyl-phenylalanine. Without such guidance, the experimentation left to those skilled in the art is undue.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) and the Intellectual Property and High Technology Technical Amendments Act of 2002 do not apply when the reference is a U.S. patent resulting directly or indirectly from an international application filed before November 29, 2000. Therefore, the prior art date of the reference is determined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

Claims 1-10, 12-16 are rejected under 35 U.S.C. 102(e) as being anticipated by US 7,045,337 B2 (Schultz et al) filed on April 19, 2002 teaches a cell composition comprising an ORS that aminoacylates an OtRNA with p-acetyl-L-phenylalanine (claim 8). No specific structure of an ORS identical to SEQ ID NO: 18 is taught in Schultz et al's however, claims 1-10, 12-16 encompass compositions comprising structurally undefined ORS molecules that can aminoacylate an OtRNA with p-acetyl phenylalanine.

The applied reference has common inventors with the instant application. Based upon the earlier effective U.S. filing date of the reference, it constitutes prior art under 35 U.S.C. 102(e). This rejection under 35 U.S.C. 102(e) might be overcome either by a showing under 37 CFR 1.132 that any invention disclosed but not claimed in the reference was derived from the inventor of this application and is thus not the invention "by another," or by an appropriate showing under 37 CFR 1.131.

Double Patenting

Claims 1-10, 12-17 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 22 and 23 of U.S. Patent No. US 6,927,042 B2 (Schultz et al [2]). Although the conflicting claims are not identical, they are not patentably

distinct from each other because Schultz et al [2] teach use of the polypeptide sequence of SEQ ID NO: 1 (identical to SEQ ID NO: 18), one ORS species derived from *M. jannaschii* claimed in claims 1-10, 12-17. Furthermore claims 22, 23 of Schultz et al.[2] teach a translation system consisting of a cell (E. coli) comprising the ORS of SEQ ID NO: 18.

The OtRNA sequences of SEQ ID NO: 21 in claims 8 and 10 in the instant specification are obvious over the composition in the method claimed in claim 23 of Schultz et al.[2] because this claim comprises SEQ ID NO: 7, a sequence that is identical to SEQ ID NO: 21 of claims 9 and 10 in the instant Application. Schultz et al.[2] teach a method of producing glycoproteins comprising the use of an ORS/OtRNA pair comprising SEQ ID NO: 18 and SEQ ID NO: 21 (identical to SEQ ID NO 1 and SEQ ID NO: 7 respectively in Schultz et al.[2])) and that the first step in the method includes incorporating an unnatural amino acid that serves as a reactive group, wherein in a preferred embodiment p-acetylphenylalanine is used. The instant invention is drawn to a composition or a cell comprising the ORS or ORS/OtRNA of SEQ ID NO: 18 (identical to SEQ ID NO: 1) and the OtRNA of SEQ ID NO: 21 (identical to SEQ ID NO: 7) used to aminoacylate an OtRNA with p-acetylphenylalanine in view of incorporating said p-acetylphenylalanine in a protein. Thus it would have been obvious to a person of ordinary skill in the art to obtain a composition or a cell comprising a composition comprising the identical ORS/OtRNA to incorporate p-acetylphenylalanine into a polypeptide of interest.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Kagnew H. Gebreyesus whose telephone number is 571-272-2937. The examiner can normally be reached on 8:30am-5:30pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Kathleen Kerr Bragdon can be reached on 571-272-0931. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Kagnew H Gebreyesus
Examiner
Art Unit 1656
August 19, 2007
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JON WEBER
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